4

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UNTREATED SYPHILIS IN THE MALE NEGRO

Observation of Abnormalities Over Sixteen Years

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THIS paper is the fourth of a series of reports[1,2,3] on the study of untreated acquired syphilis in the male Negro in Macon County, Alabama, by the Division of Venereal Disease, United States Public Health Service. Previous papers have dealt with (1) the various abnormalities found in untreated syphilitics and nonsyphilitic controls at the time of the initial examination; (2) the life expectancy of the respective groups after twelve years' observation; and (3) the natural history of syphilis, uninfluenced by treatment, with special attention to the effect of the disease on the cardiovascular system after six years' observation. The present study is a report made after sixteen years' observation and is an attempt to estimate the increment of abnormalities among untreated syphilitics and nonsyphilitic controls occurring during that sixteen-year period.

The original study population selected during the winter months of 1931-32 and 1932-33, consisted of 410 syphilitics and 201 controls presumably non-

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syphilitic, all of whom were 25 years of age or older. The presence or absence of syphilitic infection was based on history, physical examination, and qualitative serologic tests on the blood. Of the syphilitic group, 178 were given some treatment for their infection during the period of this first examination. Most of these individuals were among the younger age groups, and were given amounts of treatment varying from 1 to 15 injections of neoarsphenamine. Patients who received treatment have been dropped from consideration in the present paper. A second complete physical examination was performed in 1938-39 when 140 untreated syphilitics and 156 nonsyphilitic controls were examined. Since 1939, there has been an annual visit to Macon County by a physician for the purpose of providing a cursory physical examination and obtaining specimens of blood for serologic examination. All blood specimens have been examined in the Venereal Disease Research Laboratory at Staten Island with quantitative tests reported since 1939. In the fall of 1948, a third physical examination was performed on the 155* individuals who could be located at that time.

An important phase of the study has been the performance of autopsies on the individuals who have died. Through 1948, 140 of the number included in the study population have died, and of these 98 have been autopsied. Of those on whom autopsies have not been performed, proof of death has been established by death certificate or by information furnished by the nurse assigned to this study in the local health department or by relatives or friends of the deceased. Because of the relatively nonmigratory nature of the group, it is reasonably certain that there could not have been many deaths other than the 140 recorded. No analysis of autopsy data will be attempted in this report; a detailed account of this material will be presented at some future date.

Although the original plan of the study was to have approximately twice as many untreated syphilitics as controls (of each age), this characteristic has now been lost due principally to the administration of treatment to the younger individuals in the syphilitic group. For this reason, all findings in this presentation are based on ten-year age groups according to the age of the individuals at the time of the first examination. Table I shows how the age composition of those examined in 1948 differs from the original group selected for study.

The data presented in this table show that approximately 26 per cent of the original group of untreated syphilitics had lapsed from observation at the time of the third physical examination as compared to 35 per cent of the control group.

As previously stated, the purpose of this report is to show the development of disabling and potentially disabling conditions among untreated syphilitics and nonsyphilitic controls over the sixteen-year period 1932-48, and, if possible, to determine the increment of such abnormalities that may be attributable to syphilis. For convenience, these characteristics are put into three major classifications:

a. Death from any cause
b. Abnormal conditions of the heart and aorta
c. Abnormal conditions not involving the heart or aorta.

*Forty-five inadequately treated individuals who were examined have been excluded from this number.

TABLE I. STATUS OF THE INDIVIDUALS INCLUDED IN THE STUDY POPULATION, BY 10-YEAR AGE GROUPS, AT TIME OF THIRD PHYSICAL EXAMINATION IN 1948

STUDY POPULATION AGE IN 1932	NUMBER ORIGINALLY EXAMINED	NUMBER DEAD	NUMBER EXAMINED IN 1948	NUMBER LAPSED FROM OBSERVATION
Untreated Syphilitics:				
25–34 years	28	8	4	16
35–44 years	29	5	11	13
45–54 years	99	40	35	24
55–64 years	52	26	20	6
65 years and over	23	22	—	1
Total	231*	101	70	60
Nonsyphilitic Controls:				
25–34 years	64	5	28	31
35–44 years	34	2	17	15
45–54 years	56	12	32	12
55–64 years	26	12	7	7
65 years and over	12	9	1	2
Total	192†	40	85	67

*One individual with a dubious history of infection has been excluded from this group.

†Seven individuals who acquired syphilis since the beginning of the study and 2 individuals who may have been infected prior to the first examination have been excluded from this number.

In the classification of abnormalities the question of etiology has not been considered. Observations and measurements made by the examining physician in each of the three examinations together with his subjective findings were used to determine diagnosable conditions among the individuals. The frequency of occurrence of abnormal conditions among those examined is presented in Table II. Those not examined were assumed to have developed abnormal conditions in the same proportion as those who were examined. This assumption was not made regarding deaths because it was felt that most of the deaths in the group would occur in Macon County, and as such would be recorded. Therefore, the death rates presented in the charts are minimum.

Charts 1-5 present the comparative status at the time of the first, second, and third physical examinations of the individuals included in the untreated syphilitic and the nonsyphilitic control groups. All percentages are based on the number of individuals in the particular age-group at the time the study was initiated. Arteriosclerosis and conditions classified as "other" have not been considered in determining these percentages. Arteriosclerosis was excluded because its high prevalence among both the syphilitics and the controls tended to obscure the differences between the two groups; conditions listed as "other" were, on the whole, of a minor nature and were not reported consistently in the three examinations. The heavily shaded portion of each chart represents the percentage of the original group who have died, and is cumulative from the second

TABLE II. FREQUENCY OF ABNORMAL CHANGES FOUND IN UNTREATED SYPHILITICS AND NONSYPHILITIC CONTROLS AT PHYSICAL EXAMINATIONS IN 1932, 1938, AND 1948

ABNORMAL CONDITIONS	UNTREATED SYPHILITICS AGE IN 1932					NONSYPHILITIC CONTROLS AGE IN 1932				
	25-34	35-44	45-54	55-64	65 AND OVER	25-34	35-44	45-54	55-64	65 AND OVER
1932 (FIRST EXAMINATION)										
Number examined	28	29	99	52	23	64	34	56	26	12
Systolic hypertension (>150 mm. Hg)	5	8	34	25	19	2	3	12	—	7
Angina pectoris	—	—	—	—	—	—	—	—	—	—
Aneurysm	—	2	8	3	4	—	—	—	—	—
Aortic insufficiency	3	—	7	7	8	1	—	3	7	3
Mitral insufficiency	—	—	—	—	—	1	—	—	—	1
Arteriosclerosis	2	4	24	19	16	—	1	10	16	8
Signs of aortitis*:										
Systolic murmur (at base)	16	10	50	28	17	8	4	13	15	6
Accentuated second sound (aortic)	20	21	71	39	19	10	11	21	20	9
Increased pulsation amplitude	1	1	2	—	—	—	—	—	—	—
Arrhythmia (by auscultation)	1	—	1	—	—	—	—	—	—	4
Aortic stenosis	—	—	2	—	3	—	—	—	—	—
Psychosis	1	2	4	—	2	1	1	—	2	—
Tuberculosis (by x-ray)	3	1	—	—	2	1	—	—	1	—
Glycosuria	—	—	—	—	—	—	—	—	—	—
Cancer	—	—	—	—	—	—	—	1	—	—
Total blindness	—	—	—	1	—	—	—	—	—	—
Total deafness	—	—	—	—	—	—	—	1	—	—
Parkinson's disease	—	—	—	—	—	—	—	—	—	—
Severe skin or bone involvement	1	1	—	—	—	—	—	—	—	—
Other†	2	4	30	11	9	2	—	4	4	2

	1938 (SECOND EXAMINATION)									
Number examined	9	19	67	40	11	47	29	49	22	8
Systolic hypertension (>150 mm. Hg)	1	4	20	15	10	1	4	14	10	4
Angina pectoris	—	—	1	—	—	—	—	1	1	—
Aneurysm	—	—	4	4	2	—	—	—	1	—
Aortic insufficiency	—	1	—	2	2	1	—	1	4	—
Mitral insufficiency	—	—	1	—	1	1	—	—	—	1
Arteriosclerosis	1	10	45	37	11	1	13	27	20	8
Signs of aortitis*:										
Systolic murmur (at base)	1	6	33	26	8	12	4	17	13	4
Accentuated second sound (aortic)	3	13	48	33	11	22	13	30	10	6
Increased pulsation amplitude	2	2	24	10	4	6	3	7	6	1
Arrhythmia (by auscultation)	—	—	—	—	—	—	—	—	—	2
Aortic stenosis	—	—	—	1	—	—	—	—	1	—
Psychosis	—	2	2	2	1	2	1	3	3	—
Tuberculosis (by x-ray)	—	—	1	—	—	—	—	—	—	—
Glycosuria	—	—	—	—	—	—	—	—	1	—
Cancer	—	—	—	—	—	—	—	—	—	—
Total blindness	—	—	—	1	—	—	—	—	—	—
Total deafness	—	—	1	—	—	—	—	1	—	—
Parkinson's disease	—	—	—	—	—	—	—	—	—	—
Severe skin or bone involvement	1	1	1	—	—	—	—	—	—	—
Other†	2	4	12	9	6	5	3	6	5	4

Footnotes at end of table.

TABLE II. FREQUENCY OF ABNORMAL CHANGES FOUND IN UNTREATED SYPHILITICS AND NONSYPHILITIC CONTROLS AT PHYSICAL EXAMINATIONS IN 1932, 1938, AND 1948—CONTINUED

ARNORMAL CONDITIONS	UNTREATED SYPHILITICS AGE IN 1932					NONSYPHILITIC CONTROLS AGE IN 1932				
	25-34	35-44	45-54	55-64	65 AND OVER	25-34	35-44	45-54	55-64	65 AND OVER
	1948 (THIRD EXAMINATION)									
Number examined	4	11	35	20	—	28	17	32	7	1
Systolic hypertension (>150 mm. Hg)	—	5	17	12	—	—	4	8	4	1
Angina pectoris	—	1	4	3	—	1	1	5	2	—
Aneurysm	1	1	9	6	—	1	2	—	2	—
Aortic insufficiency	—	2	4	1	—	—	—	1	1	—
Mitral insufficiency	—	1	4	1	—	1	1	3	2	—
Arteriosclerosis	3	11	35	19	—	17	14	28	7	1
Signs of aortitis*:										
Systolic murmur (at base)	1	6	32	18	—	11	10	18	5	1
Accentuated second sound (aortic)	2	7	28	17	—	8	11	16	4	—
Increased pulsation amplitude	2	5	23	11	—	8	8	17	4	1
Arrhythmia (by auscultation)	—	—	1	3	—	2	—	—	2	—
Aortic stenosis	—	1	—	1	—	—	—	—	2	—
Psychosis	—	2	11	1	—	4	2	2	1	—
Tuberculosis (by x-ray)	—	—	—	—	—	—	—	—	1	—
Glycosuria	—	1	—	—	—	—	—	—	—	—
Cancer	—	—	—	—	—	—	—	—	—	—
Total blindness	—	—	—	2	—	—	—	—	—	—
Total deafness	—	—	1	—	—	—	—	2	—	—
Parkinson's disease	—	—	1	—	—	—	—	—	1	—
Severe skin or bone involvement	1	—	—	—	—	—	—	—	—	—
Other†	2	1	18	12	—	10	7	11	6	1

*Aortitis was diagnosed only in those cases where all three signs were found.

†"Other" includes conditions such as arthritis, rheumatism, mild osteitis or periosteitis, ulcer of stomach or duodenum, etc. These conditions have not been considered in the percentages shown in the charts.

CHARTS 1 - 5

PERCENT DISTRIBUTION OF DEATHS HAVING OCCURRED, AND DISABLING CONDITIONS FOUND AMONG UNTREATED SYPHILITICS AND NONSYPHILITIC CONTROLS AT TIME OF PHYSICAL EXAMINATION IN 1932, 1938, AND 1948, BY AGE AT TIME OF FIRST EXAMINATION

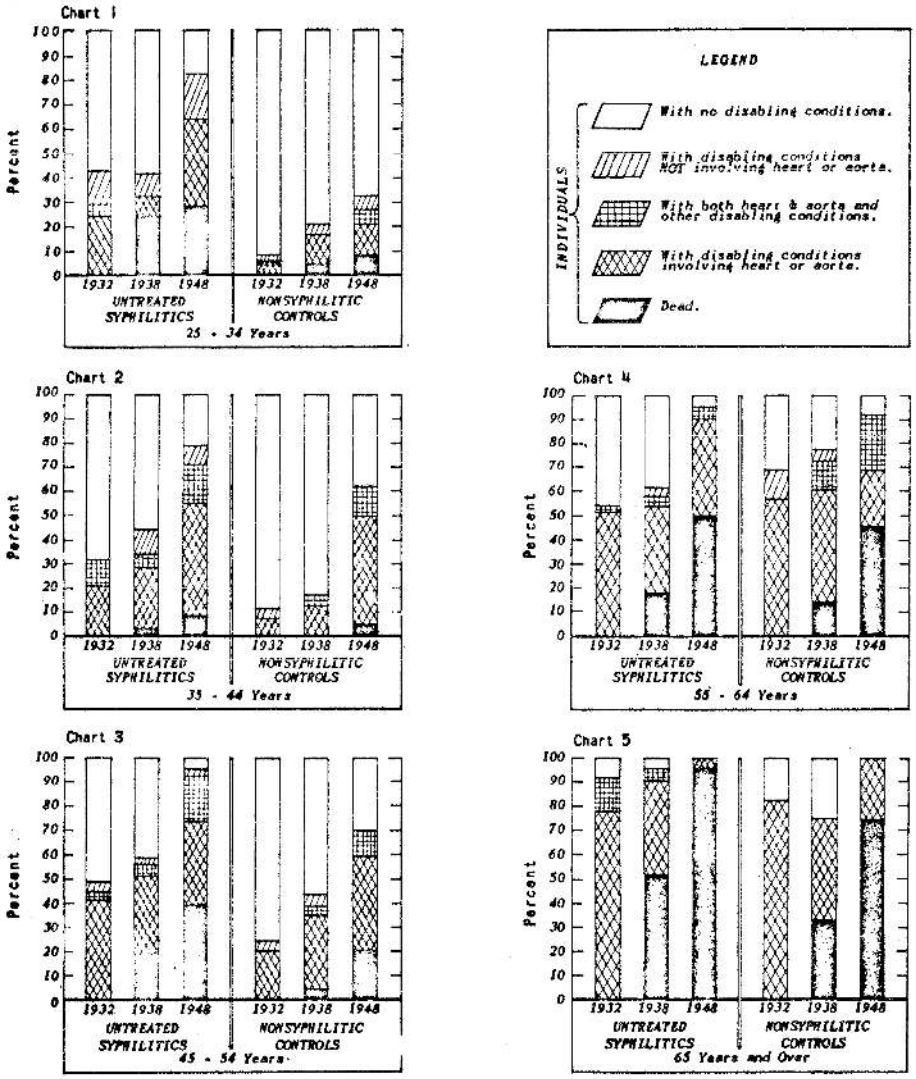

TABLE III A. FREQUENCY OF ABNORMAL CONDITIONS FOUND IN UNTREATED SYPHILITICS AND NONSYPHILITIC CONTROLS SURVIVING THROUGH 1948 WHO WERE EXAMINED IN 1932, 1938 AND IN 1948

ABNORMAL CONDITIONS	UNTREATED SYPHILITICS AGE IN 1932					NONSYPHILITIC CONTROLS AGE IN 1932				
	25-34	35-44	45-54	55-64	65 AND OVER	25-34	35-44	45-54	55-64	65 AND OVER
Number examined	2	11	33	19	—	28	17	32	7	1
Systolic hypertension (>150 mm. Hg)										
1932	—	2	8	12	—	1	2	3	3	—
1938	—	2	7	7	—	—	1	6	2	—
1948	—	4	16	12	—	—	4	8	4	1
Diastolic hypertension (>90 mm. Hg)										
1932	—	5	14	12	—	1	3	4	2	1
1938	—	4	16	10	—	5	8	14	2	1
1948	—	4	11	8	—	—	4	4	3	1
Angina pectoris										
1932	—	—	—	—	—	—	—	—	—	—
1938	—	—	—	—	—	—	—	1	—	—
1948	—	1	4	3	—	1	1	5	2	—
Aneurysm										
1932	—	—	1	—	—	—	—	—	—	—
1938	—	—	3	2	—	—	—	—	—	—
1948	—	1	9	6	—	1	2	—	2	—
Aortic insufficiency										
1932	—	—	—	1	—	1	—	—	1	—
1938	—	1	—	—	—	—	—	1	1	—
1948	—	2	4	1	—	—	—	1	1	—
Mitral insufficiency										
1932	—	—	—	—	—	1	—	—	—	—
1938	—	—	—	—	—	1	—	—	—	—
1948	—	1	4	1	—	1	1	3	2	—

Arteriosclerosis										
1932	—	2	7	9	—	—	—	3	3	1
1938	1	7	25	19	—	1	9	18	6	1
1948	2	11	33	18	—	17	14	28	7	1
Signs of aortitis:										
Systolic murmur (at base)										
1932	1	4	15	10	—	4	2	5	4	—
1938	—	3	18	14	—	9	3	9	4	1
1948	—	6	32	17	—	10	10	19	5	1
Accentuated second sound (aortic)										
1932	1	7	23	14	—	3	6	9	2	1
1938	2	10	30	16	—	19	11	20	5	—
1948	1	7	28	16	—	8	11	16	4	—
Increased pulsation amplitude										
1932	—	—	—	—	—	—	—	—	—	—
1938	—	2	11	4	—	5	1	3	1	—
1948	—	5	23	11	—	8	8	17	4	1
Arrhythmia (by auscultation)										
1932	—	—	—	—	—	—	—	—	—	—
1938	—	—	—	—	—	—	—	—	—	—
1948	—	—	—	3	—	2	—	—	2	—
Aortic stenosis										
1932	—	—	—	—	—	—	—	—	—	—
1938	—	—	—	1	—	—	—	—	1	—
1948	—	1	—	1	—	—	—	—	2	—
Psychosis										
1932	—	1	—	—	—	1	—	—	—	—
1938	—	1	1	—	—	2	—	1	1	—
1948	—	2	10	1	—	4	2	2	1	—
Tuberculosis (by x-ray)										
1932	1	—	—	—	—	—	—	—	1	—
1938	—	—	1	—	—	—	—	—	—	—
1948	—	—	—	—	—	—	—	—	1	—

TABLE III A. FREQUENCY OF ABNORMAL CONDITIONS FOUND IN UNTREATED SYPHILITICS AND NONSYPHILITIC CONTROLS SURVIVING THROUGH 1948 WHO WERE EXAMINED IN 1932, 1938, AND IN 1948—CONTINUED

ABNORMAL CONDITIONS	UNTREATED SYPHILITICS AGE IN 1932					NONSYPHILITIC CONTROLS AGE IN 1932				
	25-34	35-44	45-54	55-64	65 AND OVER	25-34	35-44	45-54	55-64	65 AND OVER
Glycosuria										
1932	—	—	—	—	—	—	—	—	—	—
1938	—	1	—	—	—	—	—	—	—	—
1948	—	1	—	—	—	—	—	—	—	—
Total blindness										
1932	—	—	—	—	—	—	—	—	—	—
1938	—	—	—	1	—	—	—	—	—	—
1948	—	—	—	2	—	—	—	—	—	—
Total deafness										
1932	—	—	—	—	—	—	—	1	—	—
1938	—	—	—	—	—	—	—	1	—	—
1948	—	—	1	—	—	—	—	2	—	—
Parkinson's disease										
1932	—	—	—	—	—	—	—	—	—	—
1938	—	—	—	—	—	—	—	—	—	—
1948	—	—	1	—	—	—	—	—	1	—
Severe skin and bone involvement										
1932	1	—	—	—	—	—	—	—	—	—
1938	1	—	—	—	—	—	—	—	—	—
1948	1	—	—	—	—	—	—	—	—	—
Other										
1932	—	2	10	5	—	2	—	2	1	—
1938	2	2	6	5	—	4	1	4	2	1
1948	2	1	17	12	—	10	7	11	6	1

to the third examination in 1948. The portions of the graphs representing abnormalities were not accumulated from one examination to the other because the progression of chronic illnesses of the type considered in this study should increase automatically (allowing for those who have died who are accounted for in the shaded portion of the chart) if the possible bias introduced by the fact that different clinicians conducted the three examinations is not too great. Since the number of abnormalities at successive examinations shows a gradual increase as indicated on the charts, rather than an erratic pattern, it would seem that such a bias is of minor degree. In Table III A is presented the frequency of disabling changes in the group of individuals who have survived through 1948 and have been under continuous observation since the beginning of the study. The results of serologic tests performed on the untreated syphilitics included in this group are shown in Table III B.

TABLE III B. RESULTS OF SEROLOGIC TESTS IN UNTREATED SYPHILITICS SURVIVING THROUGH 1948 WHO WERE EXAMINED IN 1932, 1939, AND IN 1948

RESULTS OF SEROLOGIC TESTS	UNTREATED SYPHILITICS AGE IN 1932				
	25-34	35-44	45-54	55-64	65 AND OVER
Number tested	2	11	33	19	—
1932					
Positive	2	11	33	19	—
1939*					
Negative	—	8	7	5	—
Doubtful	—	—	5	4	—
Positive	2	3	21	10	—
>1:128	—	—	—	—	—
1:128	—	—	—	—	—
1:64	1	—	2	—	—
1:32	—	—	4	—	—
1:16	—	—	2	2	—
1:8	—	2	1	4	—
1:4	—	—	3	—	—
<1:4 or undiluted	1	1	9	4	—
1948*					
Negative	—	5	17	9	—
Doubtful	1	2	4	5	—
Positive	1	4	12	5	—
>1:128	—	—	1	—	—
1:128	—	—	1	—	—
1:64	—	—	1	1	—
1:32	—	1	2	2	—
1:16	—	1	2	1	—
1:8	—	1	1	—	—
1:4	1	—	1	—	—
<1:4 or undiluted	—	1	3	1	—

*Quantitative tests were done in 1939 and 1948 at the Venereal Disease Research Laboratory, Staten Island. Results are reported as the highest dilution giving a positive reaction in the Eagle Macroflocculation Quantitative Test.

It is apparent from the charts that the percentage of individuals in each age-group dying prior to the time of second and third examinations is in every instance higher among the untreated syphilitics. Charts 1, 2, and 3 present graphically the progression of the relative amount of illness among syphilitics and controls who were 25 to 54 years of age at the time they were first observed and had advanced to 41 to 70 years of age in 1948. During these middle-age intervals, which represent the most productive and useful portion of the normal life span, a higher percentage of disability, irrespective of the number of deaths occurring, was noted at each examination for each age group among the untreated syphilitic group.

Chart - 6

THE DIFFERENTIAL OF DEATHS AND DISABLING CONDITIONS AMONG UNTREATED SYPHILITICS AND NONSYPHILITIC CONTROLS AT TIME OF PHYSICAL EXAMINATION IN 1932, 1938, AND 1948, BY AGE AT TIME OF FIRST EXAMINATION

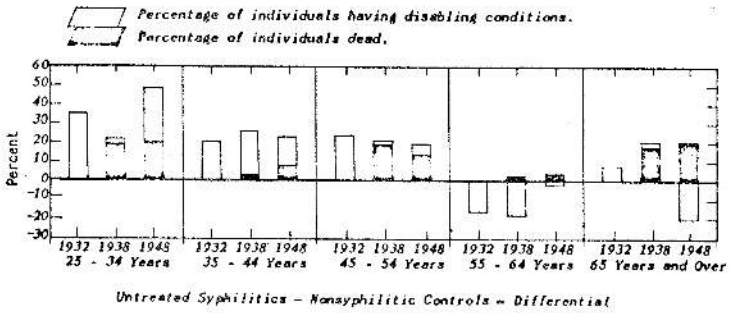

Chart 6 shows the absolute difference between the percentages for the untreated syphilitic and the nonsyphilitic control groups, and for these particular age-years might be interpreted as a rough measure of the number of deaths and the amount of disability due to the presence of syphilitic infection in the untreated group. For those individuals 55 years of age and over when first examined and advancing to 71 years and over in 1948, the comparative percentages of disability as shown in Charts 4 and 5 are not as clear-cut as those in the preceding charts. Actually, as can be seen from the differences shown on Chart 6, more disability was found among the nonsyphilitic controls at first and second examinations in the age group 55-64 years than among the untreated syphilitics. However, this difference while still in a negative direction had decreased to 1.2 per cent by 1948. In the group 65 years and over at time of first examination, the percentage of deaths among the syphilitics by 1948 exceeded those among the controls by the same amount as the disability among the controls exceeded that among the syphilitics.

In an attempt to present a general idea of the comparative amounts of mortality and disability in the two groups as a whole, the age-specific percentages for the syphilitics and the controls at time of each examination have been combined to form indices of mortality that are free from the effect of age differences. These composite percentages, based on the original study population as a stand-

ard, indicate that combined mortality and morbidity are consistently higher among the untreated syphilitics (Table IV).

TABLE IV. AGE-ADJUSTED PERCENTAGES OF DEATH AND ABNORMALITIES AMONG UNTREATED SYPHILITICS AND NONSYPHILITIC CONTROLS AT TIME OF FIRST, SECOND, AND THIRD PHYSICAL EXAMINATIONS

PHYSICAL EXAMINATIONS	UNTREATED SYPHILITICS PER CENT	NONSYPHILITIC CONTROLS PER CENT	CHI-SQUARE TEST*
First examination (1932)	47.2	26.1	Significant
Second examination (1938)	52.7	37.3	Significant
Third examination (1948)	89.1	61.1	Significant

*In Chi-square tests of differences between syphilitics and controls, $P = .01$ is used as the limit of significant deviation.

A fair estimate of the comparative rate of increase in mortality and morbidity in the two groups can also be gained from Table IV. In the untreated syphilitic group, the percentage of persons becoming disabled or dying between the years 1938 and 1948 was five times as great as the percentage becoming disabled or dying between the years 1932 and 1938; comparable figures for the controls show the percentage for the ten-year period to be only twice as large as that for the earlier six-year period.

SUMMARY

During sixteen years of observation a higher mortality rate in each ten-year age group has existed among the 231 untreated syphilitics than among the 192 nonsyphilitic controls included in this study.

Among those individuals 25 to 54 years of age at the time they were first examined, more symptomatic and potentially disabling conditions involving the heart, aorta, and other parts of the body were observed among the untreated syphilitics in each of the three physical examinations.

Among the persons 55 years of age and over when first examined, no noticeable differences in the amount of disability could be demonstrated between the two groups. (This fact might possibly be explained by the effect of natural aging processes in individuals included in the older-age groups.)

When the effect of differences in age distributions between the untreated syphilitics and the nonsyphilitic controls was removed by a standardization procedure, significant differences in the combined mortality and morbidity could be demonstrated between the two groups.

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